Functional Magnetic Resonance Imaging of Pain Transmission In the Human Spinal Cord

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Introduction: Functional magnetic resonance imaging (fMRI) is a technique utilizing the blood oxygen level dependent (BOLD) signal to elucidate neuronal activity. This tool has been used extensively to examine areas of the brain responsible for cognition, emotion, and more recently; the perception of pain. Significant processing and transmission of pain also occurs in the spinal cord and brainstem, however few researchers have used fMRI for spinal cord imaging due to a variety of technical considerations. Image degradation occurs during spinal cord fMRI due to respiratory motion artifact, CSF pulsatility, magnetic field inhomogeniety and low overall signal magnitude. Consequently, transmission of pain in the human spinal cord has yet to be examined. In this study, we sought to define patterns of fMRI activation in the human spinal cord to noxious stimuli. Specifically, our aims were to determine whether fMRI could be used to demonstrate (1) appropriate somatotopic activations in the dorsal horn of the human cervical spinal cord to noxious stimuli, and (2) lateralization of fMRI activations in the dorsal horn to noxious stimuli on the right and left upper extremity.

Methods: Healthy volunteers were recruited and subjected to a thermal pain task to determine a temperature which reliably produced 7/10 pain (0 = no pain and 10 = worst pain) in each of four sites. Subsequently, conventional and functional MRI scans were performed of their cervical spine. A 3T GE Signa whole body MR system was used to collect sagittal localizer, axial anatomic, and functional images. The subjects were imaged while experiencing 7/10 pain from a peltier heat thermode placed in right thenar, left thenar, right deltoid, and left deltoid positions. We utilized a gradient echo double-shot spiral acquisition sequence, with 12 contiguous 4mm axial slices prescribed either from C5 to C7 or C4 to C6. Other settings consisted of a 16 cm FOV, a 2000 msec TR, a 25 ms TE, and a 128 x 128 matrix. Retrospective correction for cardiac and respiration synchronized movement was performed with software created at the Stanford Center for Advanced MR Technology. All images were analyzed for activation patterns using Analysis of Functional Neuroimages (AFNI) and Brain Voyager software.

Results: Simple regression analysis revealed statistically significant ($p \leq 0.01$) voxels of activation in several regions of the spinal cord. We were able to reliably demonstrate dorsal horn activation at the cervical level consistent with the dermatome of noxious stimulation. These areas were further examined by functional connectivity algorithms within AFNI in order to minimize artifact and areas of activation outside of the spinal cord. The resulting images revealed strong activation of the ipsilateral dorsal horn of C6 and C7 with noxious stimulation of the thenar eminence. Noxious stimulation of the lateral deltoid produced

activations within the ipsilateral dorsal horn of C5 and C6. Activations correlated with ipsilateral transmission and both ascending and descending projections from the primary level of activation.

Discussion: This study provides evidence that fMRI can be used to create accurate representations of pain transmission and processing in the human spinal cord. The use of spiral k-space fMRI acquisitions combined with retrospective denoising alleviated some of the technical problems experienced in other studies. Our study was able to reveal patterns of neuronal activity within the cervical spinal cord consequent to noxious stimulation. This data contributes to creating an objective analysis of pain transmission and can be used to further investigate central changes that occur in patients with acute and chronic pain.